Journal of the American College of Cardiology Vol. 45, No. 2, 2005

Published by Elsevier Inc.
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.04.021

EDITORIAL COMMENT

Wide QRS, Narrow QRS

What's the Difference?*

Brian Olshansky, MD, FACC†
Iowa City, Iowa

Implantable cardioverter-defibrillators (ICDs) reduce the risk of death in properly selected patients. The Combined Medicare and Medicaid Services (CMS) had recommended prophylactic ICDs only for those patients with ischemic heart disease, a left ventricular ejection fraction ≤0.30, and a QRS width >120 ms (1). The QRS duration was therefore a concern.

Based on a retrospective analysis of the patients with ICDs enrolled in the PainFREE Rx II trial (2), Buxton et al. in this issue of the *Journal* (3) report that QRS width does not predict ventricular tachycardia (VT) and ventricular fibrillation (VF) events. The QRS duration did predict mortality (9% for QRS ≤120 ms vs. 15% for QRS >120 ms, p = 0.047). These intriguing data deserve a closer look.

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QRS WIDTH PREDICTS SURVIVAL, BUT ARE ALL WIDE QRS COMPLEXES THE SAME?

All interventricular conduction delays do not necessarily have the same prognostic value. The QRS duration predicts survival in patients with heart failure who have a left bundle branch block (LBBB) (4) and when the QRS is exceedingly wide (5,6) regardless of the presence or absence of coronary artery disease (4,7).

A registry of 5,517 patients (46% with ischemic heart disease) showed that LBBB and survival were associated in patients with heart failure. The LBBB was associated with an increased total mortality from any cause (hazard ratio [HR] 1.70, 95% confidence interval [CI] 1.41 to 2.05) and sudden death (HR 1.58, 95% CI 1.21 to 2.06) independent of age, type of cardiac disease, heart failure severity, and drug therapy. Right bundle branch block (RBBB) was not associated with increased mortality (8).

Hesse et al. (9) evaluated 7,073 patients referred for nuclear exercise testing excluding those with heart failure or pacemakers. After adjustment for confounders, RBBB (HR 1.5, 95% CI 1.1 to 2.1, p = 0.007) and LBBB (HR 1.5, 95% CI 1.0 to 2.0, p = 0.017) predicted mortality strongly.

DEATH IN PATIENTS WITH A WIDE QRS

Delayed ventricular activation manifested as a wide QRS is associated with poorer outcomes in patients with or without coronary artery disease. Abnormal electrical activation, associated with depolarization and repolarization abnormalities, sets the stage for re-entry and thus life-threatening ventricular arrhythmias. A direct electrophysiologic link between the QRS width, ventricular arrhythmias, and death therefore may exist.

Alternatively, delayed electrical activation can impair contractility and ventricular function. This may affect outcomes independent of cardiac arrhythmias, but the QRS width may simply reflect the presence of extensive myocardial damage without any specific causal relationship (7). The prognostic value of the QRS width may be more closely associated with the extent of the heart disease, the left ventricular ejection fraction, or heart failure symptoms.

Ischemic cardiomyopathy patients with a LBBB may have a poorer outcome because they may receive suboptimal therapy (10). These conclusions were based on outcomes of 29,585 patients with LBBB enrolled in the National Registry of Myocardial Infarction (June 1994 to March 1998). The mortality difference of patients with LBBB and myocardial infarction presenting without chest pain could be explained by undertreatment, particularly with lower use of aspirin and beta-blocker therapies. An ICD may not provide benefit depending on the purported mechanism of death.

QRS DURATION MAY PREDICT ICD BENEFIT

The QRS width seems to predict outcomes in an ICD population with coronary artery disease. In the Multicenter Automatic Defibrillator Implant Trial II (MADIT II) (11), patients with a QRS width ≥150 ms had the greatest survival benefit from ICDs, presumably because ICDs protected against fatal VT/VF events. Although not designed to address this, or any specific subanalysis, the MADIT II study (11) suggested that QRS width and gender predicted outcomes independently after ICD implantation. Complicating the issue was that outcomes based on QRS width were dependant on the cut point. When QRS duration was dichotomized at ≥120 ms, there was no meaningful difference in ICD efficacy. Ironically, men achieve the greatest benefit from prophylactic ICD implants, but this latter point, now consistent among recent ICD trials, is not addressed in any guideline (11–13).

Similar results were observed in patients with non-ischemic cardiomyopathy. The DEFibrillators In Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) trial (13), showed that patients with non-ischemic cardiomyopathy who had a QRS ≥120 ms seemed to

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

From the †Section of Cardiac Electrophysiology, University of Iowa Hospitals, Iowa City, Iowa. Dr. Olshansky is a consultant for Guidant, the Principal Investigator for the Guidant INTRINSIC RV study, a speaker for Guidant, a speaker and a consultant for Medtronic, a member of an events committee for Medtronic, and has been involved with several clinical trials for Medtronic in the past.

JACC Vol. 46, No. 2, 2005
July 19, 2005:317–9

benefit the most from best medical therapy and an ICD versus best medical therapy alone.

The Sudden Cardiac Death-Heart Failure (SCD-HeFT) trial (12) showed that patients undergoing ICD implantation who had either ischemic or non-ischemic cardiomyopathy and heart failure symptoms but whose QRS widths were ≥120 ms had lower mortality versus placebo (HR 0.67, CI 0.49 to 0.93). Those with QRS widths <120ms did not achieve the same benefit from the ICD (HR 0.84, CI 0.62 to 1.14).

These three major trials seem to indicate that the QRS width predicts benefit from an ICD, but none of these studies were designed to address this issue specifically. Based on these data, however, Nudell, a senior research analyst from Sanford C. Bernstein and Company, concluded that patients with a QRS ≥120 ms have up to a four-fold absolute mortality benefit from the ICD compared with patients with a QRS <120 ms. This type of information is considered seriously by the CMS (14).

In a sicker population, the Comparison of Medical Therapy: Pacing and Defibrillation in Heart Failure (COMPANION) trial (15), a study of patients who all had QRS widths ≥120 ms and New York Heart Association functional class III and IV heart failure symptoms, showed that those with the widest QRS complexes (>168 ms) derived the greatest benefit from a bi-ventricular (resynchronization) ICD.

The weakness of these trials, including the PainFREE RxII trial, is that these trials were not designed to address the issue of QRS duration in an ICD population. If the ICD does have specific benefit in patients with wide QRS complexes, it is likely because it treats life-threatening ventricular arrhythmias.

HOW CAN WE EXPLAIN BUXTON'S STUDY?

The Buxton et al. (3) study showed that patients with ICDs who have wider QRS complexes did not have any difference in VT/VF outcomes (3). This report included a different patient population than that in the prophylactic ICD trials (11–13). The left ventricular ejection fractions were higher in this study than the others and ranged up to 0.40. Those with the least impaired ejection fractions may represent a lower-risk group even if the QRS is wide. Buxton has cautioned us before not to rely on ejection fraction because it may not be a robust indicator of ICD benefit (16). One wonders, then, what is?

Few patients in the Buxton et al. (3) study had an LBBB. Arguably, this is the highest-risk population of those with a wide QRS complex. The study may be underpowered to detect differences between groups (3). Of those with wide QRS complexes, a nonspecific intraventricular conduction delay was the most common in Buxton's report and, based on prior data, all ventricular conduction delays are not the same. Even considering the small number of patients with LBBB in Buxton's study, however, the episode density of VT was less with an LBBB. Certainly an LBBB does not impart a more benign prognosis.

Relationships between symptoms, ejection fraction, and QRS type may better predict outcomes in these patients. An association between bundle branch block, ejection fraction, and gender is not explored here (17). Some antitachycardia pacing therapies delivered in this study may have been for nonsustained non–life-threatening VT, and this may vary by QRS width. The study could not determine this as well.

It is likely that the patients with a wide QRS width enrolled in this trial (3) were a relatively lower risk group. There is no mention of heart failure status, nor is any specific heart failure therapy described. It is likely that there is a relationship between the QRS width, episodic ventricular tachycardia, and sudden cardiac death as well as total cardiac death, but this may not be apparent because patients who are at the highest risk with a bundle branch block may have instead received a biventricular (resynchronization) ICD. With no registry data presented, there is no way to know how many patients received resynchronization therapy in lieu of a standard ICD.

Finally, it is known that survival with right ventricular pacing (causing an LBBB morphology) is even worse than an LBBB (18). In Buxton's report, 75% of patients had dual-chamber ICDs so that patients with and without a wide QRS complex may have been paced, developing a wide-paced QRS, thus leveling the playing field between patient groups.

Considering these issues, it is likely that these data do not present a fair comparison between patients with a narrow and a wide QRS width.

IS THIS REALLY AN ISSUE NOW?

Based on careful and appropriate analyses, the CMS has already concluded that a much wider range of patients can benefit from an ICD regardless of the QRS width (14). Restriction regarding QRS duration has been removed from their recommendations. The Buxton et al. (3) data confirm that patients with coronary artery disease who have a wide or a narrow QRS complex can benefit from an ICD. The article (3) addresses what now seems to be a non-issue, but is this really true? Not only does this study raise further scientific questions, but it inadvertently raises questions about how we practice medicine.

How much should we as physicians be influenced by CMS guidelines? What is the best approach for patients not eligible for CMS? What about patients who do not live in the U.S.? Although CMS guidelines may or may not represent a reasonable compilation of the present data, we must make proper recommendations to our patients regarding the best approach regardless of reimbursement issues. It is good to know that patients selected to undergo standard ICD implantation are not at the greater risk for ICD therapies for VT or VF if a wide QRS complex is present

and that another specific intervention, such as an antiarrhythmic drug, is not needed.

THE BOTTOM LINE

The QRS duration predicts outcomes of patients at risk for cardiac death but, alone, it is not a predictor of VT/VF events in patients undergoing standard ICD implantation. Criteria independent of QRS duration are now used to determine the appropriateness of ICD implantation in patients with or without coronary artery disease. Those patients with QRS complexes >120 ms who have severe heart failure symptoms and impaired ventricular function will benefit from a resynchronization ICD. Based on emerging data, it is likely that the role of the ICD and resynchronization devices will become clearer and that indications will grow.

Reprint requests and correspondence: Dr. Brian Olshansky, Cardiac Electrophysiology, University of Iowa Hospitals, 4426A JCP, 200 Hawkins Drive, Iowa City, Iowa 52242. E-mail: brian-olshansky@uiowa.edu.

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